Mediawatch

Gristle for the mill

Richard F. Harris

There's an old saying in Washington DC — making laws is like making sausage; you're better off not knowing the details. Well, that same spirit often applies to the coverage of science news. The focus is on the succulent final product rather than the process required to get there. But science journalists have found the need to take a break from that approach with one big biology story: the tale of angiostatin and endostatin.

The fate of this story was cast last May, when the *New York Times* all but declared that victory against cancer was just a few years away, thanks to Harvard's Judah Folkman and his amazing molecules (see *Mediawatch*, *Curr Biol* 1998, **8**:R438). Angiostatin and endostatin together had eradicated tumors in mice by cutting off their blood supply; humans, seemingly, would be next.

This, of course, had vast implications not only for human health but for the companies (EntreMed and Bristol-Myers Squibb) and shareholders with a stake in these potential drugs. So last November, a reporter from the *Wall Street Journal* checked up on the progress and made a rather startling discovery: Scientists at the National Cancer Institute had been unable to reproduce Folkman's results. Simply reporting that result, though, could suggest either that Folkman was a charlatan, or that the NCI scientists were all thumbs in the lab.

Of course, neither of those is the case. So the *Journal* article dug into the process of science, explaining the need for reproducibility and the trouble, sometimes, of attaining it. The stuff, it turns out, is hard to make, hard to transport, and hard to handle. "Says [Bristol-Myers Squibb] senior vice president of pharmaceutical development, Christopher Cimarusti: 'There's a difference between a lab curiosity and something you can take forward in man'. That distinction, while eminently clear to scientists such as Dr Folkman, is often lost in the public's understanding of the immensely complicated quest for a cancer cure."

Genentech scientists also tried and failed to reproduce Folkman's published results. The *New York Times* interviewed Arthur Levinson, the chief executive of Genentech, for a story that appeared one day after the *Journal*'s. "If we're doing something wrong, I would like to know what it is, because we're all hoping he's right," Dr Levinson said. "But things like this shouldn't languish too long, because the whole basis of science is reproducibility. If they can't be reproduced, at some point you have to ask yourself, are the initial claims correct?"

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By February, the suspense was too much. Again the *Wall Street Journal*, following the bouncing dollar, reported that Bristol-Myers, which has the rights to develop angiostatin, was shelving the product for the time being. An official at EntreMed, a small biotech company which also has an interest in angiostatin and endostatin (see *Gazetteer*, *Curr Biol* 1998, **8**:R633), tried to convince the *New York Times* that the Bristol-Myers announcement was a "non-event". But investors didn't buy that; the price of an EntreMed share dropped 47% in a single day.

Folkman himself by and large has avoided the media. But in February, a reporter from the *Boston Herald* sat in on a talk he gave in Boston. "Folkman said one reason other labs, including NCI, have had problems reproducing his work is that it is difficult to learn how to inject the mice with the drug without killing them. 'It takes a lot of skill to not lose a mouse,' he said. 'We spend a lot of time teaching them how to do it'." One could argue whether this comment helped resolve the mystery, or simply added to it.

National Public Radio devoted an entire story to the process of science, using the angiostatin affair as a stepping-off point. "Scientists have learned to be skeptics," reported Alison Richards. "They know that however convincing a new piece of research is, problems will arise. Failing, getting stuck and plain being wrong happen in science all the time, but you don't usually hear about it, unless, of course, you read the science journals."

The *Boston Globe*, in turn, broke some encouraging news in mid-February. NCI scientists, working in Folkman's lab, had finally been able to reproduce his results. " 'This substantiates the idea that these are technical issues' that caused the initial failures of the drug to work at the institute," NCI's Robert Wittes told the *Boston Globe*. "Now we will move to facilities in Frederick and try to reproduce the results down here."

But while reporting that EntreMed's stock value doubled on that news, the *Wall Street Journal* didn't breathe a final sigh of relief. "Independent confirmation of Folkman would be very exciting; however, these results don't qualify as such," George Yancopoulos, chief scientific officer at Regeneron Pharmaceuticals, told the *Journal*. "What worries me is that several years after the discovery of endostatin, there is still no explanation for how it works. It's still black magic." Wittes at the NCI added his note of caution: "We have to make sure it's synthesizable outside Boston."

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